REMARKS

A. Pending claims

Claims 1-18 are rejected. Claims 6, 11, 12, 14, 17 and 18 are presently amended. The amendments to the claims are made solely for grammatical purposes, and do not change the subject matter sought for patent. Claims 1-18 are pending in the case.

B. The Claims Are Unobvious Over Ison, et al.

Claims 1-18 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. patent 5,496,399 to Ison et al ("Ison"). Applicant respectfully disagrees with these rejections.

> To reject a claim as obvious, the Examiner has the burden of establishing a *prima facie* case of obviousness. *In re Warner et al.*, 379 F.2d 1011, 154 U.S.P.Q. 173, 177-178 (C.C.P.A. 1967). To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974); MPEP 2143.03.

Claim 1 recites:

> A tetracalcium phosphate (TTCP) particle comprising basic calcium phosphate whiskers on a surface of said TTCP particle; said basic calcium phosphate whiskers having a length up to about 5000 nm and a width up to about 500 nm, said basic calcium phosphate whiskers having a Ca/P molar ratio greater than 1.33, and said basic calcium phosphate whiskers having a non-stoichiometric chemical composition.

The Office action takes the position that Ison teaches:

> "calcium phosphate particles coated with precipitated mono or dibasic calcium phosphate particles (col. 4, lines 1-5). Both of these calcium phosphates are by composition basic calcium phosphates. The taught dibasic calcium phosphate has a calcium to phosphate ratio of 1 .5, which falls within the claimed range."

Applicant respectfully disagrees with these statements and submits that the Office action misinterprets Ison's "basic calcium source particles at least partially coated with a partially neutralized acidic calcium phosphate" as being the same or a substantially similar product as

Applicant's instantly claimed TTCP particle comprising "basic calcium phosphate whiskers" in addition to the other features found in the claims.

Ison appears to teach apatitic cements comprising "basic calcium source particles at least partially coated with a partially neutralized acidic calcium phosphate." Based on the reasoning set forth in the Office action, Applicant believes that the terms "acid calcium phosphate" and "basic calcium phosphate" may have been misunderstood. A "basic" calcium phosphate as defined by Ison, is a calcium phosphate having a Ca/P molar ratio > 1.33 that, when immersed in water, increases the pH of the water to > 7.0. Basic calcium phosphates familiar to those skilled in the art include, among others, tricalcium phosphate (TCP, $Ca_3(PO_4)_2$), tetracalcium phosphate (TTCP, $Ca_4(PO_4)_2O$), hydroxyapatite (HA, $Ca_{10}(PO_4)_6(OH)_2$), and the like. Ison states:

> "Basic calcium sources are known by those skilled in the art as calcium phosphates which, when added to water, raise the pH of the water to a value above 7. In general, the basic calcium sources should be more soluble than hydroxyapatite in water at pH 7. Illustrative basic calcium sources include $CaCO_3$ and basic calcium phosphates. Basic calcium phosphates that may find use in the subject invention will be those that have a calcium to phosphate ratio greater than 1.33, and include tricalcium phosphate, both α and β forms, octacalcium phosphate, tetracalcium phosphate, as well as amorphous calcium phosphates having analogous properties, and will preferably be α-tricalcium phosphate." (Ison, Col. 3, lines 31 – 43).

Similarly, an "acidic calcium phosphate," according to Ison's teachings, is a calcium phosphate having a Ca/P molar ratio < 1.33 that, when immersed in water, reduces the pH of the water to < 7.0. Examples of acidic calcium phosphates include monobasic calcium phosphate (MCP, $CaH_2(PO_4)_2$), dibasic calcium phosphate anhydrous (DCPA, $CaHPO_4$), Dicalcium phosphate dihydrate (DCPD, $CaHPO_4 \cdot 2H_2O$), and the like. In this regard Ison states:

> "Exemplary partially neutralized acidic calcium phosphates include monobasic calcium phosphate anhydrous (MCPA), monobasic calcium phosphate monohydrate (MCPM), dibasic calcium phosphate anhydrous (DCPA) and dibasic calcium phosphate dihydrate (DCPD). The coating of the basic calcium source particles may be homogeneous or heterogeneous with respect to the acidic calcium phosphate." (Ison, Col. 4, lines 1 – 8).

The Office action appears to mistakenly rely on the art-recognized name of various calcium phosphates, rather than the chemical composition thereof, in determining whether the recited calcium phosphates are acidic or basic. For example, the Office action incorrectly states:

> "Ison et al teach calcium phosphate particles coated with precipitated mono or dibasic calcium phosphate particles (col. 4, lines 1-5). Both of these calcium phosphates are by composition basic calcium phosphates. The taught dibasic calcium phosphate has a calcium to phosphate ratio of 1 .5, which falls within the claimed range. The teaching with respect to the phosphates being partially neutralized acidic refers to their pH, not their composition. The taught calcium phosphate particles can be tetracalcium phosphate (col. 3, line 41). These ratios fall within the claimed ranges." (Office action, page 2, first paragraph).

In fact, both monobasic calcium phosphate ($Ca_2(H_2PO4)_2$) and dibasic calcium phosphate ($CaHPO_4$) have Ca/P molar ratios of 0.5 and 1.0, respectively, rather than 1.5 as asserted by in the Office action and are thus by definition acidic, not basic. It appears that the prefixes "monobasic" and "dibasic" may have been misinterpreted in the Office action to refer to the alkalinity of a calcium phosphate salt, rather than the chemical composition thereof. "Monobasic" calcium phosphate is a salt formed by the replacement of a hydrogen of orthophosphoric acid (H_3PO_4) by a calcium ion (i.e., $Ca(H_2PO_4)_2$). Likewise, "dibasic" calcium phosphate refers to a salt formed by the replacement of two hydrogens of orthophosphoric acid by a calcium ion (i.e., $CaHPO_4$).

Applicant also disagrees with the assertion that "[t]he teaching with respect to the phosphates being partially neutralized acidic refers to their pH, not their composition." On the contrary, the term "acidic", as used by Ison, refers to the "calcium phosphate coating" on the surface of the dry component of Ison's two-component cement. This can be seen by the following teachings of Ison, which states:

> "The dry component of the subject compositions is prepared by combining basic calcium source particles with a dissolved acidic phosphate source in at least a partially aqueous medium, whereby the particles become partially coated with a partially neutralized acidic calcium phosphate. Prior to complete neutralization of the acidic phosphate source, the neutralization reaction is stopped through removal of the available water." (Ison, Col. 2, lines 44 – 53).

> "Alternatively, the dry component may be produced by combining a phosphoric acid solution with a basic calcium source particle slurry under conditions where partially neutralized acidic calcium phosphate precipitates on the surfaces of the basic calcium source particles." (Ison, Col. 2, lines 61-66).
>
> "The partially neutralized acidic calcium phosphate which partially coats the basic calcium source particles in the subject cement will be storage stable, i.e. not readily react with the other reactants present in the dry component of the two component cement composition, and have a calcium to phosphate ratio of at least about 1.0. The partially neutralized acidic calcium phosphate coating will be less hygroscopic and exhibit a higher thermal stability than orthophosphoric acid. Exemplary partially neutralized acidic calcium phosphates include monobasic calcium phosphate anhydrous (MCPA), monobasic calcium phosphate monohydrate (MCPM), dibasic calcium phosphate anhydrous (DCPA) and dibasic calcium phosphate dihydrate (DCPD). The coating of the basic calcium source particles may be homogeneous or heterogeneous with respect to the acidic calcium phosphate." (Ison, Col. 3, line 60 – Col. 4, line 8).
>
> "Additional calcium sources may be included in the dispersion which influence the type of acidic calcium phosphate that precipitates on the calcium phosphate particles, such as the formation of MCPM over DCPD." (Ison, Col. 7, line 65 to col. 8, line 1).

Thus, according to Ison, precipitates of acidic calcium phosphate form on the surface of basic calcium source particles. Notably, Ison teaches that the precipitated acidic calcium phosphates are only partially neutralized. Ison states:

> "Prior to complete neutralization of the acidic phosphate source, the neutralization reaction is stopped through removal of the available water." (Ison, Col. 2, lines 51-53).
>
> "The proportion of the particle surface that is coated with the partially neutralized acidic calcium phosphate will be dependent on the calcium source particle size, with larger particles having a greater proportion of their surfaces coated with the acidic calcium phosphate." (Ison, Col. 3, lines 51-55; Emphasis added).

Moreover, Ison clearly teaches that precipitated acidic calcium phosphate is coated onto particles of a basic calcium source as a result of a partial neutralization reaction. Ison states:

> "The basic calcium sources which are not to be coated with the acidic calcium phosphate will typically be soluble in the aqueous solvent and react with the acidic phosphate source in the partial reaction, e.g. as a neutralizing agent." (Ison, Col. 5, lines 26-38).

Taken together, these statements show that Ison's partially neutralized calcium phosphate coating is acidic in nature, with a Ca/P molar ratio of 0.5 (for monobasic calcium phosphate) and

1.0 (for dibasic calcium phosphate), rather than basic in nature, with Ca/P ratio of 1.5, as asserted in the Office action.

Additionally, claim 1 recites the feature "said basic calcium phosphate whiskers having a length up to about 5000 nm and a width up to about 500 nm." Applicant submits that Ison is silent on the issue of "basic calcium phosphate whiskers" having any size, dimensions or morphology. Indeed, Ison appears to be silent with regard to the morphology of the partially neutralized acidic calcium phosphate coating basic calcium phosphate source particles, and referrs to them simply as "coatings". The lack of such teachings in Ison appears to be acknowledged the Office action, which states "[t]he reference does not teach the particle size of the precipitated basic calcium phosphate particles."

Regarding claims 6 – 18, the Office action states

"[t]he coated particles are produced by mixing the calcium phosphate particles with an aqueous solution of phosphoric acid and then removing the water by drying to stop the reaction between the acid and the particles. The drying can be accomplished by any known conventional drying processes (col. 8, lines 53-67) or by heating at 70-750C (col. 9, lines 1-5). Since the taught process and that disclosed by applicants in the specification are identical, one of ordinary skill in the art would expect the taught precipitated basic calcium phosphate particles to have a size that falls within or at least overlap the claimed ranges, absent any showing to the contrary. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established." (Office action, page two, last full paragraph).

Applicant respectfully disagrees with these statements. Claim 6 recites:

A process for preparing a tetracalcium phosphate (TTCP) powder comprising TTCP particles comprising basic calcium phosphate whiskers on surfaces of said TTCP particles, said process comprising the steps:

mixing a TTCP powder with a whisker-inducing solution so that basic calcium phosphate whiskers start to grow on surfaces of TTCP particles of said TTCP powder; and

terminating the growth of said calcium phosphate whiskers by drying the whisker-inducing solution in the mixture, so that said calcium phosphate whiskers have a length up to about 5000 nm and a width up to about 500 nm, said basic calcium phosphate whiskers have a Ca/P molar

ratio greater than 1.33, and said basic calcium phosphate whiskers have a non-stoichiometric chemical composition.

Applicant respectfully disagrees with the assumption that the "coating" and method of its production disclosed by Ison would result or render obvious the claimed "whiskers or fine crystals" formed on the TTCP particles. Applicant further submits that Ison's disclosure regarding an "*acidic* coating" is distinctly different from Applicant's instantly claimed "whiskers or fine crystals" of basic calcium phosphate.

As discussed above in detail, Ison's partially neutralized acidic calcium phosphate coatings appear to be chemically distinct from Applicant's basic calcium phosphate "whiskers or fine crystals." In addition to the disparities in chemical composition between Ison's partially neutralized acidic calcium phosphate coating and the instant "whiskers or fine crystals," Applicant's whiskers or fine crystals include the feature of having "a length up to about 5000 nm and a width up to about 500 nm." As discussed above, Ison appears to be silent on this issue, a fact that appears to have been acknowledged in the Office action.

Applicant submits that the differences between the properties of the instantly claimed particles and those of the prior art rebut the presumption of *In re Best* that the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes.

In light of the arguments made above, Applicant submits that the claims are unobvious in light of the teachings of Ison. Applicant therefore respectfully requests the withdrawal of the 35 U.S.C. §103 rejections against claims 1 – 18.

C. Summary

Based on the above, Applicant submits that all claims are now in condition for allowance. Favorable reconsideration is respectfully requested.

Applicant believes no fee is required with this response. Should any fees be required or if any fees have been overpaid, please appropriately charge or credit those fees to Meyertons, Hood, Kivlin, Kowert & Goetzel, P.C. Deposit Account Number 50-1505/5937-00205/EBM

Respectfully submitted,

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